Cenata GmbH

Paul-Ehrlich-Str. 23
D-72076 Tübingen
Germany
Tel. +49 7071 565 44 430
Fax +49 7071 565 44 444
E-Mail: info@cenata.de
www.cenata.de

cenata
safe method. secure result.

Performance appraisal of the Harmony® Prenatal Test

The Harmony® Test is a prenatal screening test for the reliable detection of fetal trisomies 13, 18, and 21, by means of a simple blood test for the mother. The test can also detect DiGeorge syndrome, X- and Y-chromosomal disorders and determine the sex of the fetus.

The test can be performed from week 10+0 of the pregnancy, and eliminates the risk of miscarriage inherent in invasive methods.

Excellent detection rate

99.5% detection rate for trisomy 21 in published studies

Barely no other NIPT method has been investigated in independent clinical tests as thoroughly as the Harmony® Test has. If one summarises all studies published on singleton pregnancies, the Harmony® Test has a detection rate of 99.5%.

An overview of the Harmony® Test's trisomy 21 detection rates, for all studies published in peer-reviewed journals, can be found in the following table:

Study	Trisomy 21 cases	no. correctly detected	Detection rate
Ashoor 2012[1]	50	50	100%
Nicolaides 2012[2]	8	8	100%
Norton 2012[3]	81	81	100%
Sparks 2012[4]	36	36	100%
Verweij 2013[5]	18	17	94.4%
Juneau 2014[6]	72	72	100%
Norton 2015[7]	38	38	100%
Stokowski 2015[8]	108	107	99.1%
Total	411	409	99.5%

Reliable under treatment with heparin

because of the unique method of the Harmony® Test

Heparin therapy affects the GC content of cell-free DNA. NIPT methods based on "random massively parallel sequencing" (rMPS) show an increased test failure and incorrect results due to this problem. The Harmony® Test, however, uses the DANSR (Digital Analysis of Selected Regions) method. The gene sequences of the Harmony® Test have been pre-selected so that they are not subject to any "GC-bias". This means that even women on heparin therapy can successfully use the Harmony® Test.

Highly-qualified team of doctors

Specialists in human genetics, laboratory medicine, and obstetrics/gynecology

Cenata is comprised of a team of qualified physicians, including specialists in human genetics, laboratory medicine, and obstetrics and gynaecology. Our team is at your disposal for all questions related to prenatal diagnosis, NIPT, and the interpretation of the Harmony® Test results.

Cenata GmbH

Paul-Ehrlich-Str. 23
D-72076 Tübingen
Germany
Tel. +49 7071 565 44 430
Fax +49 7071 565 44 444
E-Mail: info@cenata.de
www.cenata.de

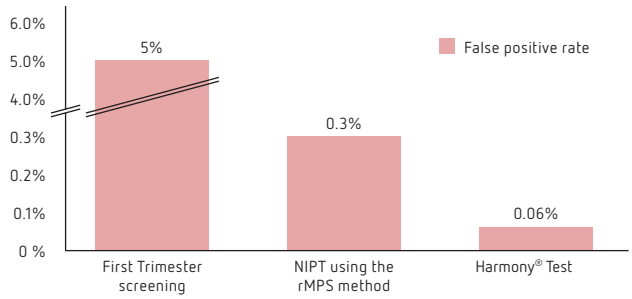
cenata
safe method. secure result.

5 times lower false positive rate

for trisomy 21 than with the rMPS method: only 0.06% instead of 0.3%

In the largest study on NIPT performed to date[7], exact data on the false positive rate of the Harmony® Test was determined. The study was carried out as a side-by-side comparison between the Harmony® Test and traditional First Trimester Screening on 18,955 normal-risk pregnancies in 35 centers in the USA, Canada, and Europe. The false positive rate was as low as 0.06%, which was five times lower than the false positive rate found for a comparable study on the rMPS method.[9]

Please note that in women above a certain age there is a higher false positive rate for sex chromosome disorders. The Harmony® Test false positive rate for trisomy 21 is 0.06%, and that for sex chromosome disorders is slightly higher.



CE certified test

for all analyzed chromosomal disorders

The FORTE_R.DLL (Fetal-fraction Optimized Risk of Trisomy Evaluation Dynamic Linked Library) software package enables the analysis of cell-free DNA (cfDNA) isolated from plasma from a pregnant woman, in order to assess the risk of fetal chromosome 13, 18, and 21 trisomies, the risk of fetal chromosome X and Y aneuploidies, and fetal sex determination. Thus, the FORTE algorithm is a major component of the Harmony® Test. The Harmony® Test analysis algorithm "FORTE" is CE certified according to the directive 98/79/EC of the European Parliament in vitro diagnostic medical devices (RL-98/79/EG, Annex II, list B) and the German Act on Medical Devices. The Harmony® Test is certified for all analysed chromosomal disorders. The blood tubes delivered with the Harmony® Test kit are certified from the manufacturer.

Very high success rate

only 1.6% of samples unanalysable, with repetition only 0.6%

The Harmony® Test is characterised by a very high success rate. Our in-house experience of 98.4% successful Harmony® Tests at the first attempt have been confirmed in a publication by the study group of Prof. Nicolaides (failure rate for singleton pregnancies, primary 1.7% and 0.7% for repeat submission).[10]

[1] Ashoor G, Syngelaki A, Wagner M, Birdir C, Nicolaides KH: Chromosome-selective sequencing of maternal plasma cell-free DNA for first-trimester detection of trisomy 21 and trisomy 18. Am J Obstet Gynecol. 2012 Apr;206(4):322.e1-5.

[2] Nicolaides KH, Syngelaki A, Ashoor G, Birdir C, Touzet G: Noninvasive prenatal testing for fetal trisomies in a routinely screened first-trimester population. Am J Obstet Gynecol. 2012 Nov;207(5):374.e1-6.

[3] Norton ME, Brar H, Weiss J, Karimi A, Laurent LC, Caughey AB, Rodriguez MH, Williams J 3rd, Mitchell ME, Adair CD, Lee H, Jacobsson B, Tomlinson MW, Oepkes D, Hollemon D, Sparks AB, Oliphant A, Song K: Non-Invasive Chromosomal Evaluation (NICE) Study: results of a multicenter prospective cohort study for detection of fetal trisomy 21 and trisomy 18. Am J Obstet Gynecol. 2012 Aug;207(2):137.e1-8.

[4] Sparks AB, Struble CA, Wang ET, Song K, Oliphant A: Noninvasive prenatal detection and selective analysis of cell-free DNA obtained from maternal blood: evaluation for trisomy 21 and trisomy 18. Am J Obstet Gynecol. 2012 Apr;206(4):319.e1-9.

[5] Verweij EJ, Jacobsson B, van Scheltema PA, de Boer MA, Hoffer MJ, Hollemon D, Westgren M, Song K, Oepkes D: European non-invasive trisomyevaluation (EU-NITE) study: a multicenter prospective cohort study for non-invasive fetal trisomy 21 testing. Prenat Diagn. 2013 Oct;33:996-1001.

[6] Juneau K, Bogard PE, Huang S, Mohseni M, Wang ET, Ryvkin P, Kingsley C, Struble CA, Oliphant A, Zahn JM: Microarray-based cell-free DNA analysis improves noninvasive prenatal testing. Fetal Diagn Ther. 2014;36:282-286.

[7] Norton ME, Jacobsson B, Swamy GK, Laurent LC, Ranzini AC, Brar H, Tomlinson MW, Pereira L, Spitz JL, Hollemon D, Cuckle H, Musci TJ and Wapner RJ (Next-Study): Cell-free DNA Analysis for Noninvasive Examination of Trisomy. N Engl J Med. 2015, Apr 1, DOI: 10.1056/NEJMoa1407349.

[8] Stokowski R, Wang E, White K, Batey A, Jacobsson B, Brar H, Balanarasimha M, Hollemon D, Sparks A, Nicolaides K, Musci TJ. .: Clinical performance of non-invasive prenatal testing (NIPT) using targeted cell-free DNA analysis in maternal plasma with microarrays or next generation sequencing (NGS) is consistent across multiple controlled clinical studies. Prenat Diagn. 2015 Sep 1.

[9] Bianchi DW, Rava RP, Sehnert AJ: DNA sequencing versus standard prenatal aneuploidy screening. N Engl J Med. 2014 Aug 7;371(6):578. doi: 10.1056/NEJMc1405486).

[10] Bevilacqua E, Gil MM, Nicolaides KH, Ordoñez E, Cirigliano V, Dierickx H, Willems PJ, Jani JC. Performance of screening for aneuploidies by cell-free DNA analysis of maternal blood in twin pregnancies. Ultrasound Obstet Gynecol. 2014 Oct 9. doi: 10.1002/uog.14690.